

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	)	Confirmation No. 9884
	)	
David SIDRANSKY <i>et al.</i>	)	
	)	Group Art Unit: 1642
Application Serial No.: 10/821,203	)	
	)	Examiner: C.M. Joyce
Filed: April 8, 2004	)	
	)	
For: BRAF MUTATION T1796A IN THYROID	)	
CANCERS	)	Atty. Dkt No.: 001107.00463

**DECLARATION UNDER RULE 131**

We, David Sidransky, MingzhaoXing, and Yoram Cohen, declare:

1. We are the named inventors on the subject application.
2. Claims 1-5, 7, and 9 stand rejected as anticipated by or obvious over Kimura et al., "High prevalence of BRAF mutations in thyroid cancer: genetic evidence for constitutive activation of the RET/PTC-RAS-BRAF signaling pathway in papillary thyroid carcinoma," Cancer Res. 2003 Apr 1;63(7):1454-7.
3. The independent claim 1, upon which claims 2-5, 7, and 9 depend, is directed to a method for distinguishing malignant papillary from benign thyroid samples. The method comprises: determining presence of a T → A transversion at nucleotide 1796 of *BRAF* according to SEQ ID NO: 1 in a thyroid sample of a human. The presence of the transversion indicates a malignant papillary neoplasm and absence of the transversion indicates a benign neoplasm or sample.
4. We conceived and reduced the claimed invention to practice prior to April 1, 2003.

5. We conducted experiments, obtained data, wrote a manuscript describing the experiments and data, and submitted the manuscript to a scientific journal, all prior to April 1, 2003. One journal that we submitted a manuscript to is *Nature Genetics*. This journal archives its manuscript submissions and makes them available on-line to the original submitters. Attached as **Exhibit 1** is the letter which we sent to *Nature Genetics* requesting that they review our manuscript and publish it. The attached letter was downloaded from the *Nature Genetics* website. (The date has been redacted.) Attached as **Exhibit 2** is a copy of the manuscript that we submitted to *Nature Genetics*. The attached copy was downloaded from the *Nature Genetics* website. Attached as **Exhibit 3** is a copy of the index sheet from the *Nature Genetics* website, indicating the dates and disposition of the manuscript. (The dates have been redacted.) As evidenced by the index sheet the manuscript was never revised.
6. The content of the manuscript demonstrates that we had actually conceived of and reduced to practice a method comprising determining presence of a T → A transversion at nucleotide 1796 of *BRAF* according to SEQ ID NO: 1 in a thyroid sample of a human, wherein presence of the transversion indicates a malignant papillary neoplasm and absence of the transversion indicates a benign neoplasm or sample.
7. Specifically, the manuscript details testing 54 thyroid samples. Page 1, lines 17. Exon 15 of *BRAF* was amplified and then digested with endonuclease TspRI to identify *BRAF* T1796A mutations. Page 1, lines 19-20. Such mutations were identified in 60% of papillary thyroid carcinomas (page 2, lines 4-5) but in no benign thyroid conditions, follicular thyroid carcinomas, medullary thyroid carcinomas, or Hurthle cell carcinomas (page 2, lines 9-12). These data are also shown in Table 1 (page 5). An example of the experimental method and results is shown in Figure 1a.

8. We hereby declare that all statements made herein of our knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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Date

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David Sidransky

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Date

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MingzhaoXing

13.4.07  
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Date

  
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Yoram Cohen